was prepared through use of the software program "PatentIn" provided by the PTO. The information contained in the computer readable disk is identical to that of the paper copy. This amendment contains no new matter. Applicant submits that this amendment, the accompanying computer readable sequence listing, and the paper copy thereof serve to place this application in a condition of adherence to the rules 37 C.F.R. § 1.821-1.825.

Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,
DORSEY & WHITNEY LLP

Dated: 8/2/02

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Filed under 37 C.F.R. Section 1.34(a)

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Paragraph beginning at page 6, line 15, has been amended as follows:

— Figures 7A-B show identification of cryptic intron recognition sequences (underlined), polyadenylation signals (bold), and RNA instability sequences "ATTTA" (italics) in (7A) (SEQ ID NO:15) the original MSP1.42 FUP and (7B) (SEQ ID NO:16) FVO DNA sequences.—

Paragraph beginning at page 7, line 28, has been amended as follows:

— A "p42 polypeptide," as defined herein, is a polypeptide comprising a p42 amino acid sequence, including fragments and variants thereof, of the Plasmodium major merozoite surface protein gp195. The NtMSP1.42S polypeptide is included within the definition of a p42 polypeptide and comprises a p42 polypeptide encoded by an NtMSP1.42S nucleic acid sequence (see e.g., SEQ ID NO: 1), which differs from the p42 nucleic acids (see e.g., SEQ ID NO:13 of Fig. ~~12~~ 10). The "NtMSP1.42S" nucleic acid comprises a nucleic acid sequence in which one or more codons have been substituted with codons encoding the same or similar amino acid such that the NtMSP1.42S mRNA transcript is preferentially recognized by the tRNAs present in a tobacco plant host cell. One NtMSP1.42S amino acid sequence, as set forth in SEQ ID NO:2, differs from the amino acid sequence encoded by the p42 nucleic acid sequence set forth in Fig. ~~12~~ 10, by residues at positions 1-8, 376-379, and residues at positions 381-383. The NtMSP1.42C polypeptide is further included within the definition of a p42 polypeptide and comprises a p42 polypeptide encoded by an NtMSP1.42C nucleic acid (see e.g., SEQ ID NO: 3) wherein the upstream signal sequence of NtMSP1.42S has been substituted by 24 consensus nucleotides optimized for transgenic plant translation initiation (Helliwell et al., (1995) Plant Mol. Biol. 29:621) encoding a consensus sequence for ribosomal binding and a translation initiation site (Di Sansebastiano et al. (1998) Plant Journal. 15:449), comprising nucleotides 1-1149 of SEQ ID NO:3 (see e.g., amino acid residues 1-383 of SEQ ID NO: 4).—

Paragraph beginning at page 8, line 14, has been amended as follows:

— The NtMSP1.42S nucleic acids (see e.g., nucleotides 1-1149 of SEQ ID NO:1) encoding the p42 and NtMSP1.42S polypeptides as described supra (see e.g., amino acid residues 1-383 of SEQ ID NO:2) are included within the definition of p42 nucleic acids. The NtMSP1.42S nucleic acids differ significantly from other previously described p42 nucleic acids (see, e.g., SEQ ID NO:13 of Fig. ~~12~~ 10) by the substitution of one or more codons with codons encoding the same or similar amino acids. One NtMSP1.42S nucleotide sequence, as set forth in SEQ ID NO:1, differs from the nucleotide sequence as set forth in Fig. ~~12~~ 10 at nucleotide positions 1-24, 222, 1126-1137, and 1141-1149. The NtMSP1.42S mRNA transcript, transcribed from the NtMSP1.42S nucleotides, is preferentially recognized by the tRNAs present in the tobacco plant host cell expression system. This preferential recognition results in enhanced translation of the NtMSP1.42S transcripts and enhanced production of the NtMSP1.42S polypeptide. The NtMSP1.42C nucleic acids (see, e.g., nucleotides 1-1149 of SEQ ID NO:3) are further included within the definition of p42 nucleic acids and comprise nucleic acids encoding NtMSP1.42C polypeptides (see e.g., amino acid residues 1-383 of SEQ ID NO:4) wherein the 24 nucleotides encoding the upstream signal sequence have been substituted by the 24 consensus nucleotides optimized for transgenic plant translation initiation (Helliwell et al., supra) encoding a consensus sequence for ribosomal binding and a translation initiation site (Di Sansebastiano et al., supra). —

Paragraph beginning at page 26, line 21, has been amended as follows:

— For example, useful linkers include glycine polymers $(G)_n$, glycine-serine polymers (including, for example, $(GS)_n$, $(GSGGS)_n$ (SEQ ID NO:17) and $(GGGS)_n$ (SEQ ID NO:18), where n is an integer of at least one), glycine-alanine polymers, alanine-serine polymers, and other flexible linkers such as the tether for the shaker potassium channel, and a large variety of other flexible linkers, as will be appreciated by those in the art. Glycine and glycine-serine polymers are preferred since both of these amino acids are relatively unstructured, and therefore may be able to serve as a neutral tether between components. Glycine polymers are the most preferred as glycine accesses significantly more phi-psi space than even alanine, and is much less restricted than residues with longer side chains (see Scheraga, Rev. Computational Chem. III73-

142 (1992), expressly incorporated by reference). Secondly, serine is hydrophilic and therefore able to solubilize what could be a globular glycine chain. Third, similar chains have been shown to be effective in joining subunits of recombinant proteins such as single chain antibodies.—

Paragraph beginning at page 37, line 23, has been amended as follows:

—New constructs utilizing the MSP1.42 FVO sequence, which lack the FUP MSP1.42 coding region cryptic intron splice sites (e.g., Example 1), were evaluated. The MSP1.42 FVO sequence also was modified to enhance translation by the addition of plant-specific translation initiation codons, a ribosomal binding site and optimization of the AUG translation start site within the 5' upstream region. Constructs were prepared which contained either an endoplasmic reticulum retention signal (HDEL (SEQ ID NO:19)) or a hexa-Histidine region within the 3' terminus of MSP1.42 FVO. The majority of transgenic plants recovered in experiments containing the MSP1.42 FVO sequence had an insert of the expected 1.2 kB size although one anomalous plant contained a larger insert. Despite these modifications, these transgenic plants also produced low levels of MSP1.p42-related mRNA products of approximately half the expected size. Furthermore, these plants did not contain any material reacting with antibodies against native MSP1.42. Therefore, although integration of the complete MSP1.42 gene appeared to occur with these new constructs, the sequence alterations intended to enhance translation and the omission of cryptic intron splice sites within the FVO allele were still insufficient for gene expression.—

On page 44, immediately preceding the claims, the enclosed text entitled "Sequence Listing" was inserted into the specification.